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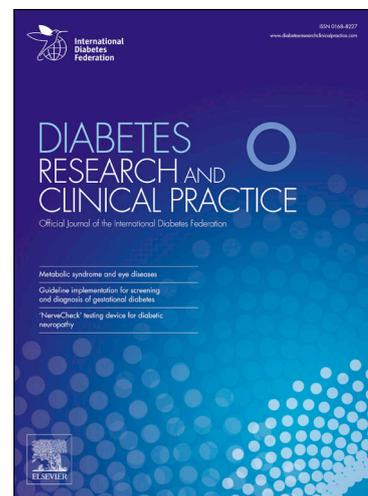
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Cost and Cost-Effectiveness of mHealth interventions for the prevention and control of Type 2 Diabetes Mellitus: A Systematic Review

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Highlights:

- A pre specified protocol was registered on the Prospective Register of Systematic Reviews
- To the best of our knowledge this is the first systematic review on this topic
- The quality of evidence was assessed using the CHEERS checklist
- The majority of studies identified were partial economic evaluations
- There was difficulty in comparing results due to study heterogeneity

ABSTRACT

The prevalence of type 2 diabetes mellitus continues to rise and simultaneously technology has contributed to the growth of MHealth interventions for its prevention, monitoring and management. This systematic review aimed to summarize and evaluate the quality of the published evidence on cost and cost-effectiveness of mHealth interventions for T2DM. A systematic literature search of PubMed, EMBASE, and Web of Science was conducted for papers up to end of April 2019. We included all partial or full economic evaluations providing cost or cost-effectiveness results for mHealth interventions targeting individuals diagnosed with, or at risk of, type 2 diabetes mellitus. Twenty-three studies met the inclusion criteria. Intervention cost varied substantially based on the type and numbers or combination of technologies used, ranging from 1.8 INT \$ to 10101.1 INT \$ per patient per year. The studies which presented cost effectiveness results demonstrated highly cost-effective interventions, with cost per QALY gained ranging from 0.4 to 62.5 percent of GDP per capita of the country. The quality of partial economic evaluations was on average lower than that of full economic evaluations. Cost of mHealth interventions varied substantially based on type and combination of technology used, however, where cost-effectiveness results were reported, the intervention was cost-effective.

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1.0 INTRODUCTION

1.1 Burden of Type 2 Diabetes Mellitus (T2DM)

In 2017, diabetes was ranked as the fourth leading cause of disability globally[1]. The health consequences of diabetes cause a marked loss of productivity and economic burden to patients, healthcare providers and country's economies, mounting to 1.8% of the global gross domestic product (GDP) and 12% of the global health expenditure in 2018 [2,3]. Over 80% of yearly deaths due to diabetes occur in developing countries causing drastic economic consequences compared to their developed counterparts [4]. Diabetes is notoriously difficult to control with only about 50% of patients reaching their treatment targets[5]. There are multifactorial explanations for this, including the challenges T2DM poses on patients' habits surrounding diet and exercise. Many patients demonstrate low willingness to change their perceptions and actions to alter their undesirable lifestyle habits[6,7]. Moreover, treatment plans often consist of multiple daily pharmacological interventions which contribute to poor medication adherence[8].

1.2 MHealth interventions

Mobile health (mHealth) uses technology to encourage patients' lifestyle modification and medication adherence by providing portable, every-day interventions to empower patients and encourage them to adhere to their management plans[9]. The rise of mHealth has heavily correlated with the exponential growth in internet access which has allowed for the creation of wireless healthcare opportunities combining patient empowerment with the convenience of mobile devices [10,11]. MHealth interventions are becoming prominent amongst several medical specialties encompassing preventative, curative and chronic management goals. Additionally, mHealth reduces geographic related disparities in health care by removing physical barriers to accessing medical information and providing individuals a "virtual" platform. Successful MHealth interventions have shown to significantly reduce hospital inpatient admissions and prompt a 63% reduction in number of admission days[12].

1.3 MHealth and T2DM

MHealth interventions targeting diabetes have shown clinical effectiveness in both the prevention and management of T2DM [13–15]. Management based interventions have proven to be particularly successful at reducing haemoglobin A_{1c} (HbA_{1c}) levels amongst people with T2DM [14]. A meta-analysis investigating mobile phone interventions for glycaemic control demonstrated that among 22 trials there was a statistically significant improvement in glycaemic control amongst users of the online intervention[16]. Similarly, another review found that glycaemic control results were significant amongst T2DM when mobile text messaging interventions were combined with an internet based intervention[17]. MHealth interventions have proven to be low cost and cost-effective across various medical specialties [18,19]. Economic evidence is crucial to guide policy makers and funders towards implementing mHealth interventions. Nevertheless, there is a large gap in the literature analysing the costs and cost-effectiveness of mHealth interventions addressing T2DM [20]. To the best of our knowledge, there is currently no published literature summarising the cost or cost-effectiveness of mHealth interventions targeting the prevention and control of T2DM. This study aims to systematically review, analyse and summarise the published evidence on the cost and cost-effectiveness of mHealth interventions for T2DM, as well as, to assess the quality of the published evidence.

2.0 METHODS

Our systematic review was reported in accordance with the 2015 PRISMA statement[21]. Our protocol was registered with the International Prospective Register of Systematic Reviews in January 2019 (PROSPERO registration number CRD42019123476) and it is published elsewhere[22].

2.1 Search Strategy

Electronic database search on MEDLINE(Pubmed), EMBASE, and Web of Science was conducted including all relevant studies published up to the 30th of April 2019. The keyword search was divided into four main groups: “mHealth”, “diabetes”, “cost effectiveness” and “prevention or management”. These were combined together using the Boolean operator “AND” and included their respective synonyms using the operator “OR”. The initial search strategy was developed for use on MEDLINE and then adapted for subsequent databases. The full key words used are shown in Appendix 1.

2.2 Inclusion & Exclusion criteria:

We included all primary studies published in English from January 1995 to end of April 2019. The included studies were both partial or full economic evaluations for mHealth interventions targeting the prevention or management of T2DM. Partial economic evaluations were defined as evaluations that provide the costs of an intervention, but do not compare the costs with an alternative intervention or to the outcomes of the intervention[23]. Costs reported as costs of the intervention from either the provider (eg design and implementation), patient or societal perspective will be included in the review. Full economic evaluations are defined as those that do compare the costs of the intervention with one or more alternative interventions and relate these to the measured outcomes. Full economic evaluations include cost-effectiveness analysis (CEA), cost utility analysis (CUA), cost benefit analysis (CBA), cost minimisation analysis and cost-consequence analysis[23]. All papers including mHealth interventions that were targeting patients at risk of or diagnosed with T2DM were included in this review. MHealth interventions were defined as interventions that included use of the internet, mobile devices or computers. Exclusion Criteria encompassed papers that were not published in a peer reviewed journal or not in the English language. Unpublished documents and grey literature like conference papers, dissertations, and patents were excluded.

2.3 Study Selection and data extraction

The relevant papers from the literature were managed in Mendeley to facilitate the screening and selection process. The papers were screened for any duplicates, then for relevance using their titles and, thirdly, their abstracts. The remaining studies had their full text screened for our inclusion and exclusion criteria. The remaining studies were included in our results. The included studies were assessed for their quality of reporting evidence and their data was extracted and summarised. Two reviewers (G.R., A.H.) independently extracted data from the included studies using our data extraction tool adapted from existing guidelines and other review articles of economic evaluations[23–25]. Using this tool we extracted the general and economic features of the papers including the characteristics of the intervention, population and reported outcomes.

2.4 Quality assessment

The quality of reporting the economic evaluation evidence was assessed using the Consolidated Health Economic Evaluation Reporting Standards (CHEERS)[26] checklist for full economic evaluations and using a Modified version of CHEERS checklist for partial economic evaluation. Our Modified CHEERS checklist includes relevant elements from the CHEERS checklist and some modified elements used by previous researchers[22,27]. Both GR and AH independently assessed the included papers against these checklists and any discrepancies were resolved by discussion and involvement of third author (HHB). Papers that were recognized as meeting the checklist item were given “yes” for that category and “no” if they did not meet the checklist item. A “part” score was given if the paper met some of the checklist requirements, whilst an “n/a” was given if this was not relevant to the specific paper. Overall, papers who met over 75% of the checklist item were considered to be of high quality, those meeting 50% to 75% of the checklist they were regarded to be of moderate quality, and if they met less than 50% of checklist items they were labelled as being of poor quality.

2.5 Cross-study comparison and interpreting cost effectiveness results

To allow for comparability across time and settings we converted all costs and cost-effectiveness ratios to 2018 international dollars (INT\$) using purchasing power parity, consumer price indexes and currency exchange rates from the World Bank Open Database³⁹. To further judge the cost-effectiveness results, national and international cost-effectiveness threshold were used. In the United Kingdom a threshold of £20,000 to £30,000[28], and in the USA US\$50,000 per Quality Adjusted Life Years (QALY) gained were used[29]. For other settings, the World Health Organisation (WHO)[30] and Wood’s et al.’s[31] cost-effectiveness thresholds were applied. WHO state that an intervention is highly cost-effective if cost-effectiveness ratio (cost per disability-adjusted life years- or DALY averted) is less than the gross domestic product (GDP) per capita and is cost-effective if it is between one and three times the GDP per capita[30]. Wood’s et al.’s[31] have estimated cost effectiveness thresholds for each country which are much lower than the WHO threshold and are around 50% GDP per capita. Therefore, based on this threshold, an intervention will be cost-effective if incremental cost-effectiveness ratio (ICER) is less than the country GPD per capita[32].

3.0 RESULTS

Our systematic database search identified the following number of studies from the three databases:

- Pubmed: 2309 items found on 4th May 2019
- EMBASE: 1744 items found on 6th May 2019
- Web of Science: 1223 items found on 5th May 2019

The study selection is shown in Figure 1 using the preferred reporting items for a systematic review and meta-analysis protocol (PRISMA-P) flowchart [21]. At the end of the selection process we had 23 final studies to include in our systematic review. .

Figure 1: Study selection process- See uploaded file

3.1 General Features of included papers

The characteristics of the included 23 studies are summarised in Table 1 and reported in detail in Additional File 1. Of the studies identified the majority, 15 (65%) were partial economic evaluations. There were eight full economic evaluations identified, of which three (13%) were CEA reporting the costs of an intervention per a natural outcome unit, for example, changes in HbA1C. We also identified five (22%) CUA reporting their outcomes using QALYs. No cost benefit analysis was identified in our review. Fourteen (61%) of the included papers were randomised control trials. Eleven (78%) of these compared the mHealth intervention to usual care whilst other three compared it to a non-mHealth intervention. The three extra interventions that all participants received in certain studies included a 6 month exercise program, printed diabetes self-management support materials and periodic lifestyle incentives, and three home visits over 1 year from a care coordinator[33–35]. The majority of papers were published within the last 10 years (74%) as there has been an increasing number of cost-effectiveness and costing papers published in this area more recently as represented in Figure 2.

The different types of technologies included video consultations, online blood glucose recorder, phone calls, text messages, emails, website use or a heart rate monitor. Of these, the online blood glucose recorder was the most popular with 11 out of 23 (48%) studies incorporating it into their mHealth intervention. The next most popular mHealth interventions were phone calls (39%) and text messages (30%). Interestingly, four of the mHealth interventions were supplemented by non-mHealth components. These results are represented in Appendix 2.

Table 1: Summary of characteristics of included papers

Feature	N	%
Type of economic evaluation		
CEA	3	13
CUA	5	22
Partial Economic Evaluations	15	65
Study Design		
RCT	14	61
Mixed RCT & Modelling	2	9
Cohort	3	13
Modelling	4	17
Perspective evaluated		
Patient	2	9
Healthcare Provider	18	78
Societal	3	13
Time horizon		
<= 1 year	9	39
1-10 years	12	52
over 10 years/lifetime	2	9
Type of Economic outcome		
QALY	3	13
Cost or Savings per patient	14	61
Willingness to Pay	1	4
ICER	5	22
Intervention Type		
Preventative	1	4
Management	21	91
Mixed	1	4
Type of data used		
Primary data	18	78
Secondary data	5	22
Type of sensitivity analysis		
One-way/Univariate	4	17
Probabilistic analysis / Multivariate	5	22
Not performed/specified	14	61
Low / Middle / High Income Country		
High	18	78
Middle	5	22

CEA, cost-effectiveness analysis; CUA, cost-utility analysis; RCT, randomised controlled trial; QALY, quality adjusted life year; ICER, incremental cost effectiveness ratio.

Figure 2: Publication count per Year

3.2 Full Economic Evaluations

The cost-effectiveness ratios of the eight full EEs ranged from INT\$ 28.4 to INT\$1,871 saving per patient per year and from INT\$ 245 to INT\$ 39,167 per QALY gained. As per the WHO cost-effectiveness threshold all five studies reporting cost per QALY gained were cost-effective as ICER as % of GDP per capita ranged from 0.4 to 62.5%. Of these, the two studies that used one mHealth technology reported cost per QALY gained had values of 0.9% and 0.4% of their respective countries' GDP per capita [36,37]. Whilst the one study that integrated two mHealth technologies reported costs per QALY gained equivalent to 7% of the GDP per capita (2018) showing high cost effectiveness based on the WHO thresholds [38]. This intervention involved a weekly nurse led telephone service that would remotely consult patients using an online glucose monitor. Those that integrated three mHealth technologies reported QALY gained values of equivalent to 47.2% and 62.5% of their respective countries' GDP per capita [39,40].

Only one study, by Wong et al, focused on the prevention of T2DM [36]. They created a text messaging education service targeted for patients with, or at risk of, T2DM. This intervention costed INT\$ 254 per QALY gained and resulted in cost savings of INT\$ 28 per patient each year. This was on the lower end of costs compared to the seven interventions based on the management of T2DM. Interestingly, all of the full EEs were based in high income countries. As shown in Appendix 2, three of these studies included mHealth interventions supplemented by non-mHealth components. Two of these included extra visits by a clinician whereby one intervention included an extra clinic visit with a doctor that year and the second included an extra three home visits by a care coordinator over the year [33,41]. Whilst one intervention was supplemented by printed educational material on healthy lifestyle [34].

These results are represented in Table 2.

Table 2: Reported cost-effectiveness of Full EE interventions

Reference	Setting	Type of mHealth intervention	ICER or Unit Cost in 2018 (int\$)	UNIT of Cost Reported	ICER as % OF GDP Per Capita (2018)
One Technology					
Fasterholdt et al. 2018 [41]	Denmark	• Video Calls	1871.0	cost saving/patient/ year	
			3133.2	Incremental cost per 1% change in the amputation rate	
Schechter et al. 2016 [33]	USA	• Phone Calls	241.2	cost/patient/year	
			597.1	cost per % of HbA1C decreased	
Varney et al. 2016 [37]	Australia	• Telephone call coaching Service	233.3	Cost/patient/year	
			665.4	Cost/QALY gained	0.9
Wong et al. 2016 [36]	Hong Kong	• SMS service	245.1	Cost/QALY gained	0.4
			28.4	cost saving/patient/year	
Two Technologies					
Gordon et al. 2014 [42]	Australia	• Weekly phone calls • Online glucose level record keeper	534.1	cost saving/patient /year	
			3966.8	Cost/QALY gained	7.7
Warren et al. 2017 [34]	Australia	• Online glucose record keeper • Video calls	2259.0	Cost/ difference in % point HbA1C change	
			688.9	cost saving/patient/year	
Three Technologies					
Glimer et al. 2019 [39]	Mexico	• Online glucose record keeper • SMS service	9429.8	Cost/QALY gained	47.2

		<ul style="list-style-type: none"> • Video Educations 			
Handley et al. 2008 [40]	USA	<ul style="list-style-type: none"> • Telephone Service 	39166.8	Cost / QALY gained	62.5
		<ul style="list-style-type: none"> • Online glucose level recorder 	947.3	cost/person/year	

ICER, incremental cost effectiveness ratio; Int\$, international dollar; GDP, gross domestic product; HbA1C, glycated haemoglobin; QALY, quality adjusted life year; SMS, short message service;

3.3 Partial Economic Evaluations

Out of the fifteen partial EEs, nine presented results as cost per patient per year which ranged from INT \$ 1.8 to INT\$10,110. Four studies presented results as cost savings per patient per year which ranged from INT\$ 61 to INT\$7,232. Two studies reported other outcomes; one study represented costs as willingness to pay per month and another as cost per home telemedicine unit. These results are presented in Table 3. All but one of the partial EEs focused on the management of T2DM; Fottrel et al's intervention included both preventative and management interventions and costed on the lower end of the included studies at INT\$ 7 per patient per year.

The interventions that integrated only one type of technologies reported costs per patient per year ranged from INT\$ 1.8 to INT\$ 241. Those that reported costs as costs savings per patient each year ranged from INT\$ 1,249 to INT\$ 7,232. Three studies included mHealth interventions incorporating two types of technologies and five studies incorporated three types of technologies. The most expensive intervention reported costs of INT\$ 10,110 cost per patient per year and integrated three types of mHealth technology. The majority of studies were based in high income countries with only three studies set-in middle-income countries. Only one of these interventions was supplemented by a non-mHealth component, which consisted of an exercise program[35].

Table 3: Reported costs of Partial EE interventions

Author & Year	Setting	Type of mHealth intervention	COST in 2018 (int\$)	UNIT of Cost Reported
One Technology				
Chen et al. 2018 [43]	China	<ul style="list-style-type: none"> • SMS Service 	10.1	cost/patient/year
Deng et al. 2015 [44]	Canada	<ul style="list-style-type: none"> • Online glucose level recorder 	240.7	cost/patient/year
Fottrell et al. 2019 [45]	Bangladesh	<ul style="list-style-type: none"> • SMS/Voice message 	7	cost/person/year
Haddad et al. 2014 [46]	Iraq	<ul style="list-style-type: none"> • SMS Service 	1.8	cost/patient/year
Islam et al. 2015 [47]	Bangladesh	<ul style="list-style-type: none"> • SMS Service 	57.3	WTP / month for diabetes SMS
Levin et al. 2013 [48]	Denmark	<ul style="list-style-type: none"> • Diabetes video consultations 	7232.1	cost saving/patient /year
Salzsieder et al. 2011 [49]	Germany	<ul style="list-style-type: none"> • Online glucose level recorder 	1249.3	cost saving/patient /year
Two Technologies				
Biermann et al. 2002 [50]	Germany	<ul style="list-style-type: none"> • Telephone consultation • Online glucose level recorded 	894.5	cost saving/patient/year
Fritzen Et al. 2019 [51]	Germany	<ul style="list-style-type: none"> • Online glucose level recorder • SMS Service 	61.1	cost saving/patient /year
Katalenich et al. 2015 [52]	USA	<ul style="list-style-type: none"> • Online glucose record keeper • SMS service 	723.3	cost/patient/year
Three Technologies				
Glasgow et al. 1997 [53]	USA	<ul style="list-style-type: none"> • One single touch screen computer session • Phone calls • Educational Videotape 	214.4	cost/patient/year

Kesavadev et al. 2012 [54]	India	<ul style="list-style-type: none"> • Online glucose record keeper • SMS service • Email reminders 	10.2	cost/patient/year
Marios et al. 2012 [35]	Australia	<ul style="list-style-type: none"> • Heart rate monitor • Weekly phone calls 	1513.0	cost/patient/year
Moreno et al. 2009 [55]	USA	<ul style="list-style-type: none"> • Online glucose record keeper • Video calls • Interactive website 	10110.1	cost/patient/year
Shea et al. 2006 [56]	USA	<ul style="list-style-type: none"> • Online glucose record keeper • Video calls • Interactive website 	4403.6	cost/ home telemedicine unit

ICER, incremental cost effectiveness ratio; Int\$, international dollar; WTP, willingness to pay; QALY, quality adjusted life year; SMS, short message service.

3.3 Quality of reporting evidence

Full Economic Evaluations

The findings show that on average compliance with the CHEERS checklist was much greater for full economic evaluations compared to partial economic evaluations. No study adhered to all checklist items. Amongst the full economic evaluations for 19 out of the 24 checklist items there was 75% or more compliance. The remaining five checklist points were the greatest areas of weakness for the full economic evaluations (Figure 4). The seven weakest item checklist points were numbers 9, 11, 12, 13, 14, 15 and 16. All of these points are within the Methods subsection of the CHEERS checklist. Moreover, none of the four economic evaluations based on modelling fully justified why they chose that specific model and only half of them described the assumptions underpinning their model. To summarize, 6 out of 8 (75%) of the included full economic evaluations were deemed of high quality according to the CHEERS checklist and the remaining 2 (25%) were of moderate quality.

Figure 3: Quality of Full Economic Evaluations

Partial Economic Evaluations

Amongst the partial economic evaluations, only 1(7%) was of high quality, whilst 3 (20%) were of moderate quality and 11 (73%) were assessed to be of poor quality. Four out of 15 (27%) of the included studies complied with 50% of the modified CHEERS checklist requirements. This immediately highlights that the partial economic evaluations were on average of lower quality than the full economic evaluations. However, majority of the studies (n=14, 93%) mentioned the perspective of their analysis and all studies abided to point 14 by summarizing their findings and discussed the limitations of their study.

The major areas of weakness amongst partial economic evaluations were points 8-12a and 13. Only one (7%) of the papers reported those checklist points. The full assessment of quality of evidence is reported in Appendix 3.

Figure 4: Quality of Partial Economic Evaluations

4.0 DISCUSSION

The current study aims to systematically review and summarise the research surrounding the costs and cost-effectiveness of mHealth interventions targeting T2DM. Our results have shown that, overall, the quality of reporting was weak among both partial and full economic evaluations, however, poorer amongst partial evaluations. The cost varied based on the type of intervention, the number of technologies integrated and whether it was combined with a non-mHealth component. Importantly, all those that reported cost-effectiveness results showed that the interventions were highly cost effective.

The first objective of this review was to summarise the literature on the cost and cost effectiveness of mHealth interventions for diabetes. This review has highlighted a limited number of full economic evaluations in this area. We identified only eight full economic evaluations in the literature. The majority of studies were from high-income countries with none set in low-income settings. This may reflect a technology disparity in lower income countries, but simultaneously represents an opportunity to begin to evaluate mHealth within newer health care systems. We also noticed that 16 out of 23 (70%) studies were RCTs and it is encouraging to find that economic outcomes are increasingly being reported alongside trials, however, further efforts are needed to produce full cost-effectiveness evidence alongside trials.

It seems that the mHealth interventions with one technology had lower costs with reported costs per patient per year ranging from INT\$ 1.8 to INT\$ 241.0 compared to those with two technologies (INT\$ 61.1 to INT\$ 894) and three technologies (INT\$ 10.2 to INT\$ 10110.1). Interestingly, patients often state too much complexity of the mHealth intervention[57]. Our results seem to agree that often a simple mHealth intervention using only one type of technology may be the most user friendly and also least costly. Another interesting consideration is that the majority of interventions (92%) we found were targeting the management of diabetes with only two interventions focusing on the prevention of the disease. Evidence surrounding preventative mHealth interventions remains extremely limited. Further exploration into the cost-effectiveness of preventative mHealth interventions for diabetes is warranted.

The second objective of this review was to evaluate the quality of reporting costs and cost-effectiveness evidence. Poor methodological quality is known to be a major area of weakness for healthcare economic evaluations[58,59]. This review has highlighted that the methodology of economic evaluations necessitates improvement, especially amongst partial evaluations or costing studies. In these studies, only 1 out of 15 papers (7%) provided evidence on how they identified or valued resources, the dates of costs included, the discount rates used or provided a detailed breakdown of costs. Without being able to explore the costing methodology of a costing paper it remains difficult to scrutinize its generalizability. Lower CHEERS scores might be expected amongst partial economic evaluations as for 12 out of 15 (80%) the costs were not the primary outcome of the study. However, this highlights the need for readers to be cautious when accepting costing results from partial economic evaluations as they may be methodologically flawed. This emphasises the importance of systematic reviews and quality reviews such as this paper. Moreover, a verified modified CHEERS checklist for partial economic evaluations should be developed.

In conducting this review, we faced a few challenges with the data which are worth mentioning. The first challenge was the heterogeneity amongst the studies due to differences in reported cost, outcome measures, currency and settings. Any review of both full and partial economic evaluations will invariably experience this heterogeneity. We increased comparability by converting reported unit costs and cost-effectiveness results into a common international

currency and base year. We also acknowledge that specialized databases for economic evaluations were not used.

Secondly, due to limited relevant papers, we were unable to conduct a sub-analysis the cost of MHealth interventions by income level and geographical region. Individuals living in rural areas often experience the effects of the medical “brain drain” and need to travel further to see a doctor. This leaves them at greater risk of having less exposure to health education and having a higher risk of developing conditions like diabetes[60]. Having more economic data on the impact of mHealth interventions in rural areas could lead to promising results to tackle health inequalities[61]. Evidence has shown that telemedicine interventions for diabetes can significantly reduce the blood sugar, blood pressure and cholesterol of patients in rural underserved communities[62]. Until now, only one study has previously demonstrated that an SMS based mHealth intervention in a rural Bangladeshi community increased knowledge about diabetes[45]. Further exploration into the success of mHealth interventions within rural communities is paramount.

Limitations of our review are due to our search strategy. We only included published evidence in the English language, so we acknowledge there will be some publication bias within our results. We also want to highlight that the generalizability of our results needs to take into consideration the country setting, type of intervention and our methodology used to convert costs into 2018 international dollars.

5.0 CONCLUSION

This review is the first to evaluate and summarise this area of the literature. Findings point to growing economic evidence on mHealth intervention targeting T2DM, although a limited number of full economic evaluation or cost-effectiveness studies exist. The cost of mHealth interventions varied substantially based on type and combination of technology used. However, where cost-effectiveness results reported, the intervention was highly cost-effective. Continued efforts towards integration of high-quality economic evaluations within trials are required to strengthen the economic evidence for mHealth interventions targeting diabetes in different populations, in particular in low- and middle-income countries.

Author Contributions

HHB conceptualized the study. GR carried out the literature review of which the strategy was reviewed by AH and HHB. GR and AH assessed the quality of included studies independently. HHB was involved if there were any discrepancies in the assessment of the study quality. GR wrote the first draft of the manuscript which was individually reviewed by both AH and HHB. All authors have approved the final version of the manuscript.

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FIGURE LEGEND:

Figure 1: *Study selection process*

Figure 2: *Publication Count per Year*

Figure 3: *Quality of Full Economic Evaluations*

Figure 4: *Quality of Partial Economic Evaluations*

Journal Pre-proofs

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Appendix 1

Key Words used for Literature search

Search strategy key words

((((((((((m-health) OR ehealth) OR mhealth) OR MeSH) OR mobile health) OR telemedicine) OR e-health) OR application) OR app) OR electronic health)).

AND ((((((((((diabetes) OR Type 2 Diabetes) OR Diabetes Mellitus) OR T2DM) OR DM2) OR impaired glucose tolerance) OR insulin resistance) OR pre-diabet*) OR impaired fasting tolerance).

AND (((((((((((cost effectiv*) OR cost-effetiv*) OR cost benefit) OR cost-benefit) OR cost-utility) OR cost utility) OR cost analysis) OR cost-analysis) OR economic evaluation) OR cost*) OR cost outcome)).

AND (((((((((((((((monitor*) OR control*) OR management) OR prevention) OR risk reduction) OR lifestyle modification) OR exercis*) OR physical fitness) OR bariatric surgery) OR metformin) OR diet) OR weight loss) OR food) OR obesity) OR BMI.

Appendix 2: Type of mHealth Intervention

Study (Author, year)	Number of mHealth technologies used	Description of MHealth technology	Combination with a non mHealth component? (Yes/no)	Description of the non-mHealth component
Biermann et al, 2002	2	<ul style="list-style-type: none"> • Telephone consultation • Online glucose level record keeper 	No	-
Chen et al. 2018	1	<ul style="list-style-type: none"> • SMS Service 	No	-
Deng et al. 2015	1	<ul style="list-style-type: none"> • Online glucose level recorder 	No	-
Fasterholdt et al 2018	1	<ul style="list-style-type: none"> • Diabetes video consultations 	Yes	One outpatient consultation
Fottrell et al. 2019 Bangladesh	1	<ul style="list-style-type: none"> • SMS/voice message service 	No	
Fritzen Et al. 2019	2	<ul style="list-style-type: none"> • Online glucose level record keeper 	No	
Glimer et al. 2019	3	<ul style="list-style-type: none"> • Online glucose record keeper • SMS service • Video Educations 	No	
Glasgow et al 1997	3	<ul style="list-style-type: none"> • One single touch screen computer session • phone calls • videotape intervention for each participant 	No	
Gordon et al. 2014	2	<ul style="list-style-type: none"> • Weekly phone calls • Online glucose level recorder 	No	
Haddad et al. 2014	1	<ul style="list-style-type: none"> • SMS service 	No	
Handley et al 2008	3	<ul style="list-style-type: none"> • Telephone Service • Online glucose level recorder 	No	
Islam et al 2015	1	<ul style="list-style-type: none"> • SMS Service 	No	
Katalenich et al 2015	2	<ul style="list-style-type: none"> • Online glucose record keeper • SMS service 	No	
Kesavadev et al 2012 (its published in 2012 not 2011)	3	<ul style="list-style-type: none"> • Online glucose record keeper • SMS service • Email reminders 	No	
Levin et al 2013	1	<ul style="list-style-type: none"> • Diabetes video consultations 	No	
Marios et al 2012	3	<ul style="list-style-type: none"> • Heart rate monitor • Weekly phone calls 	Yes	An exercise program
Moreno et al 2009	3	<ul style="list-style-type: none"> • Online glucose record keeper • Video calls • Interactive website 	No	
Salzsieder et al 2011	1	<ul style="list-style-type: none"> • Online glucose record keeper 	No	
Schechter et al 2016	1	<ul style="list-style-type: none"> • Phone calls 	Yes	Printed education material
Shea et al 2006	3	<ul style="list-style-type: none"> • Online glucose record keeper • Video calls • Interactive website 	No	
Varney et al 2016	1	<ul style="list-style-type: none"> • Telephone call coaching Service 	No	
Warren et al 2017	2	<ul style="list-style-type: none"> • Online glucose record keeper • Video calls 	Yes	Three home visits over 1 year from a care coordinator
Wong et al 2016	1	<ul style="list-style-type: none"> • SMS service 	No	

mHealth, mobile health; SMS, short message service.

Appendix 3: Full quality assessment

CHEERS items	Fasterholdt et al 2018	Glimmer et al 2019	Gordon et al 2014	Handley et al 2008	Schechter et al 2016	Varney et al 2016	Warren et al 2017	Wong et al 2016
1	Green	Green	Green	Green	Green	Green	Red	Green
2	Green	Green	Green	Green	Pink	Green	Green	Green
3a	Green	Green	Green	Green	Green	Green	Pink	Green
3b	Green	Green	Green	Green	Green	Green	Green	Green
4	Green	Pink	Green	Green	Green	Green	Green	Red
5	Green	Green	Green	Green	Green	Green	Green	Green
6	Green	Green	Green	Green	Green	Green	Green	Green
7	Green	Green	Green	Green	Green	Green	Green	Green
8	Green	Green	Green	Green	Green	Green	Pink	Green
9	Green	Green	Green	Red	Red	Green	Red	Green
10	Pink	Green	Green	Green	Green	Green	Green	Green
11	Pink	White	Red	Pink	Green	Green	Pink	Green
12	White	Green	Red	Pink	Red	Green	Red	Red
13a	Red	White	White	Green	Pink	White	Pink	White
13b	White	Green	Green	White	White	Green	White	Pink
14	Green	Green	Pink	Red	Green	Pink	Green	Green
15	White	Pink	Pink	White	White	Pink	Pink	Red
16	White	Green	Red	White	White	Green	Pink	Pink
17	Green	Green	Green	Pink	Green	Green	Red	Green
18	Green	Green	Green	Pink	Green	Green	Green	Green
19	Green	Green	Green	Pink	Pink	Green	Green	Green
20a	Green	White	White	Green	Green	White	Green	Green
20b	White	Green	Green	White	White	Green	White	Green
21	Green	Green	Green	Red	Green	Green	Green	Red
22	Green	Green	Green	Green	Green	Green	Green	Green
23	Green	Green	Green	Green	Green	Green	Green	Green
24	Green	Green	Green	Green	Green	Green	Green	Green
Quality	High	High	High	Moderate	High	High	Moderate	High

- a) Tabulated CHEERS checklist results for full economic evaluations (n=8)
(Green=Yes, Pink = Partly, Red=No, White=n/a)

CHEERS items	Biermann et al. 2002	Chen et al. 2018	Deng et al 2015	Fottrell et al. 2019	Fritzen et al 2019	Glasgow et al 1997	Haddad et al. 2014	Katalenich et al 2015	Kesavadev et al 2012	Levin et al 2011	Marios et al 2012	Moreno et al 2009	Salzsieder et al. 2011	Islam et al 2015	Shea et al 2006
1	Green	Red	Green	Pink	Green	Pink	Red	Red	Green	Green	Red	Green	Red	Green	Red
2	Green	Green	Green	Green	Pink	Pink	Pink	Pink	Green	Pink	Pink	Pink	Pink	Green	Pink
3	Green	Green	Green	Green	Red	Red	Green	Green	Green	Green	Green	Pink	Green	Green	Green
4	Green	Green	Pink	Green	Green	Green	Pink	Pink	Pink	Green	Green	Red	Green	Pink	Green
5	Green	Pink	Pink	Green	Pink	Green	Green	Green	Pink	Green	Green	Pink	Green	Red	Green
6	Green	Green	Green	Green	Green	Green	Pink	Green	Green	Green	Green	Green	Green	Green	Green
7	Green	Green	Pink	Green	Red	Green	Green	Green	Pink	Green	Pink	Pink	Green	Green	Pink
8	Green	Red	Red	Pink	Red	Pink	Red	Red	Red	Red	Red	Red	Red	Red	Red
9	Green	Red	Red	Red	Pink	Pink	Pink	Red	Pink	Pink	Red	Pink	Pink	Red	Red
10	Green	Red	Red	Pink	Pink	Red	Red	White	Pink	Red	Pink	Red	Red	Red	Red
11	Green	Red	Red	Red	Red	Red	Red	Pink	Red	Red	Red	Red	Red	Red	Red
12a	Pink	Pink	Pink	Red	Red	Green	Red	Pink	Pink	Pink	Red	Pink	Pink	Pink	Red
12b	Green	Green	Green	Green	Pink	Green	Red	Green	Green	Red	Green	Green	Green	Green	Red
13	Green	Red	Red	Red	Red	Red	Red	Pink	Red	Red	Red	Red	Red	Red	Red
14	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green
15	Green	Green	Red	Green	Green	Pink	Red	Green	Green	Red	Green	Green	Green	Green	Red
16	Green	Green	Red	Red	Green	Red	Red	Green	Green	Red	Red	Green	Red	Red	Red
Quality	High	Moderate	Poor	Moderate	Poor	Poor	Poor	Poor	Moderate	Poor	Poor	Poor	Poor	Poor	Poor

b) Tabulated CHEERS Checklist result for partial economic evaluations (n=15)
 (Green=Yes, Pink = Partly, Red=No, White=n/a)

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